AAOS Clinical Practice Guideline Summary

Preventing Venous Thromboembolic Disease in Patients Undergoing Elective Hip and Knee Arthroplasty

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Abstract

This guideline supersedes a prior one from 2007 on a similar topic. The work group evaluated the available literature concerning various aspects of patient screening, risk factor assessment, and prophylactic treatment against venous thromboembolic disease (VTED), as well as the use of postoperative mobilization, neuraxial agents, and vena cava filters. The group recommended further assessment of patients who have had a previous venous thromboembolism but not for other potential risk factors. Patients should be assessed for known bleeding disorders, such as hemophilia, and for the presence of active liver disease. Patients who are not at elevated risk of VTED or for bleeding should receive pharmacologic prophylaxis and mechanical compressive devices for the prevention of VTED. The group did not recommend specific pharmacologic agents and/or mechanical devices. The work group recommends, by consensus opinion, early mobilization for patients following elective hip and knee arthroplasty. The use of neuraxial anesthesia can help limit blood loss but was not found to affect the occurrence of VTED. No clear evidence was established regarding whether inferior vena cava filters can prevent pulmonary embolism in patients who have a contraindication to chemoprophylaxis and/or known VTED.

This clinical practice guideline was approved by the American Academy of Orthopaedic Surgeons on September 24, 2011.

The complete guideline, which includes all tables, figures, and appendices, is available at http://www.aaos.org/research/guidelines/VTE/VTE_guideline.asp

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Overview and Rationale

This clinical practice guideline was approved by the American Academy of Orthopaedic Surgeons (AAOS) on September 24, 2011. It is based on a systematic review of published studies on preventing venous thromboembolic disease (VTED) in patients undergoing elective hip or knee arthroplasty and supersedes a prior guideline from 2007 on a similar topic (*AAOS Clinical Guideline on Prevention of Symptomatic Pulmonary Embolism [PE] in Patients Undergoing Total Hip and Knee Arthroplasty*[1,2]). In addition to providing practice recommendations, this guideline also highlights gaps in the literature and areas that require future research.

The purpose of this clinical practice guideline is to help improve treatment based on the current best evidence. Current evidence-based practice standards demand that physicians use the best available evidence in their clinical decision making. To effectuate this, this clinical practice guideline consists of a series

of systematic reviews of the available literature regarding various aspects of patient screening, risk factor assessment, and prophylactic treatment against VTED, as well as the use of postoperative mobilization, neuraxial agents, and vena cava filters. These systematic reviews were conducted on studies written in English and published during or after 1970. The review was conducted on articles that were full manuscripts, published in peer-reviewed journals, and of the highest available evidence. The AAOS staff and the VTED work group systematically reviewed the available literature and, subsequently, the following recommendations were based on a rigorous, standardized process.

Musculoskeletal care is provided in many different settings by many different providers. We created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. This guideline should not be construed as including all proper methods of care or as excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

This guideline represents a cross-sectional view and may become outdated as new evidence becomes available. The AAOS may revise this guideline in accordance with new evidence, changing practice, rapidly emerging treatment options, or new technology. This guideline will be updated or withdrawn in 5 years in accordance with the standards of the National Guideline Clearinghouse.

Methods

The methods used to develop this clinical practice guideline were designed to combat bias, enhance transparency, and promote reproducibility. Their purpose is to allow interested readers the ability to inspect all of the information the work group used to reach all of its deci-

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sions and to verify that these decisions are in accord with the best available evidence.

To develop the clinical practice guidelines, the work group first formulated a set of preliminary recommendations that specified what should be done in whom, when, how often, or for how long. These were intended to function as the questions for systematic review by the AAOS research team.

Once all relevant published articles that met predetermined inclusion criteria were assembled and graded by level of evidence, the work group then provided a final recommendation of strong (good-quality evidence), moderate (fair-quality evidence), weak (poor-quality evidence), inconclusive (insufficient or conflicting evidence), or consensus (in the absence of reliable evidence, the workgroup makes a recommendation based on clinical opinion).

The guideline includes 10 recommendations and 4 additional subcategorized recommendations. One of the 10 recommendations is graded as strong, three as moderate, one as weak, and one as inconclusive. Four recommendations are based on consensus.

All tables, figures, and appendices, as well as the details of the methods used to prepare this guideline, are included in the full clinical practice guideline, which is available at **http://www.aaos.org/research/guidelines/VTE/VTE_guideline.asp**

The draft of this guideline was subject to peer review and public commentary, and it was approved by the AAOS Evidence Based Practice Committee; Guidelines and Technology Oversight Committee; Council on Research, Quality Assessment, and Technology; and the Board of Directors.

Recommendations

Recommendation 1

We recommend against routine postoperative duplex ultrasonography screening of patients who undergo elective hip or knee arthroplasty.

Grade of Recommendation: Strong

Rationale: We cannot recommend the routine use of ultrasound for the screening of patients after knee or hip arthroplasty for deep vein thromboembolism (DVT). The best available evidence comes from two randomized controlled studies, both of high quality and moderate applicability, that compared routine ultrasound screening to not screening.[3,4] The control group was prolonged prophylaxis in one study and a sham ultrasound in the other. In the ultrasound groups, treatment of asymptomatic DVTs was based on the ultrasound findings. Neither study found a statistically significant difference between symptomatic pulmonary embolism (PE) rates in the ultrasound-screened and -unscreened patients, despite the fact that they had adequate statistical power.

These negative findings may arise from the shortcomings of ultrasound. Eight diagnostic studies of high quality and moderate applicability evaluated the diagnostic performance of ultrasound, using venography as a reference standard.[5-13] Results varied by study. The results suggest that although ultrasound is a good "rule in" test for DVT, it is not a good "rule out" test.

Similar results are found when screening is accomplished using venography. Two retrospective comparative studies of low quality and moderate applicability compared the results of patients who were screened for DVT by venography against the results of patients who were not screened.[14,15] Treatment of asymptomatic DVT varied according to venographic results. Rates of readmission for PE and DVT did not significantly differ between those who received screening venography and those who did not.

The available evidence also suggests that D-dimer is not a useful screening test for DVT after arthroplasty. Three screening studies, one of high quality and two of moderate quality, and all of moderate applicability, evaluated the diagnostic performance of D-dimer.[5-7] Two used ultrasound as the reference standard, while one used venography.

One study of high quality and moderate applicability evaluated the diagnostic performance of magnetic resonance venography compared with venography.[8] These data indicated that magnetic resonance venography may be a good "rule in" test but not a good "rule out" test. Given the lack of utility of ultrasound for diagnosis of unsuspected DVTs and the lack of any commonly available alternative screening test with greater utility, we do not recommend routine screening for DVT in the postoperative hip and knee arthroplasty patient population.

Recommendation 2

Patients undergoing elective hip or knee arthroplasty are already at high risk for venous thromboembolism. The practitioner might further assess the risk of venous thromboembolism by determining whether these patients had a previous venous thromboembolism.

Grade of Recommendation: Weak

Current evidence is not clear about whether other factors increase the risk of venous thromboembolism in patients undergoing elective hip or knee arthroplasty and, therefore, we are unable to recommend for or against routinely assessing these patients for these factors.

Grade of Recommendation: Inconclusive

Rationale: Patients undergoing elective hip or knee arthroplasty are at high risk of VTED. Only one risk factor, previous history of VTED, has sufficient evidence indicating

that some of these patients may be at even higher risk.

The relevant evidence comes from two studies that evaluated patients with a personal history of VTED: one medium and one low strength.[16,17] The study by Pedersen et al[16] of more than 68,000 patients found a relative risk of 8.1, and the study by Warwick et al[17] of more than 14,000 found a hazard ratio of 4.92 for postoperative VTED in patients with a previous history of VTED.

Twenty-nine studies addressed whether patients with one or more other potential risk factors have higher rates of VTED. The studies were all of low or very low strength. A statistically significant increase in VTED resulting from these other risk factors that confer an increased risk of VTED in other surgeries was not found in studies of hip or knee arthroplasty patients. This might be because these other VTED risk factors confer a lower overall risk than does the surgery itself. Therefore, their effects may not be seen against the relatively high background risk already being experienced by patients receiving elective hip or knee arthroplasty. Thus, we are unable to recommend further risk stratification based on these factors.

No data specific to hip or knee arthroplasty were found addressing many potential risk factors, and in many instances where they were found, the data were of very low quality and contradictory. Data from other surgical patients were found also to be of very low quality and therefore were unreliable.

Recommendation 3

Patients undergoing elective hip or knee arthroplasty are at risk for bleeding and bleeding-associated complications. In the absence of reliable evidence, it is the opinion of this work group that patients be assessed for known bleeding disorders, such as hemophilia and for the presence of active liver disease.

Grade of Recommendation: Consensus

Current evidence is not clear about whether other factors increase the chance of bleeding in these patients and, therefore, we are unable to recommend for or against using them to assess a patient's risk of bleeding.

Grade of Recommendation: Inconclusive

Rationale: Complications related to the soft-tissue envelope around the surgical site of bleeding, and the effects of bleeding on functional outcomes, are a significant concern. A hematoma can lead to a periprosthetic joint infection (with its associated morbidity) or to joint stiffness and a compromised functional outcome. Although these potential risks have not been traditionally addressed as a part of other guidelines, given the seriousness of these concerns, this work group believed it necessary to address them.

We found very few data that addressed risk factors for bleeding in patients undergoing elective hip or knee surgery. Two studies of very low quality addressed patients with hemophilia, with the sole comparative study finding it to be a significant predictor of hemarthrosis.[18,19] One comparative study of very low quality addressed cirrhosis of the liver and found it to be a significant predictor of perioperative blood loss.[20]

Therefore, patients with a known bleeding disorder or active liver disease may have an increased risk for bleeding. Evaluating patients for these factors has minimal cost and low risk to the patient; we believe that these actions are consistent with the current practice of most orthopaedic surgeons. Therefore, issuing a consensus-based recommendation for carefully evaluating each patient to ensure that the risk of total hip and total knee arthroplasty is proportional to their functional deficit is warranted. Recommendation 6 discusses the recommended thromboprophylaxis strategy for these patients.

Evidence about whether other factors affect the risk for bleeding in these patients is unclear. Four low-quality studies among nonarthroplasty surgical patients did not find convincing evidence that preoperative coagulation screening predicts postoperative bleeding:[18,19,21,22] (1) bleeding time predicted blood loss in one of three studies; (2) fibrinogen predicted blood loss in one of three studies; (3) platelet count predicted blood loss in one of six studies; and (4) prothrombin time predicted blood loss in one of six studies.

In other very low-quality (and, therefore, unreliable) studies of nonarthroplasty surgical patients, (1) thrombocytopenia was a significant predictor of postoperative intracranial hematoma among intracranial surgery patients, (2) a history of gastrointestinal (GI) bleed was not a significant predictor of postoperative upper GI bleeding among nonulcer surgery patients, (3) a history of bleeding with previous surgery did predict excessive bleeding among cardiac bypass patients, and (4) epistaxis and a history of bleeding with dental extraction each did not predict major bleeding among type 1 von Willebrand disease patients undergoing surgery.

No data were found addressing the other risk factors.

The data on hemorrhage-related complications are also sparse. Three low-quality and 14 very low–quality studies addressed whether patients with one or more of the potential risk factors have higher rates of hemorrhage-associated complications. Low hemoglobin levels and more complex revision procedures did predict a higher

risk of transfusion, but none of the factors studied could be directly tied to hemorrhage-associated complications, such as deep periprosthetic joint infection.

Due to the inconclusive evidence regarding other risk factors for bleeding or hemorrhage-associated complications among elective hip and knee arthroplasty patients, we are unable to recommend for or against further risk stratification.

The clinician should be aware of established contraindications against the use of individual anticoagulant agents.

Recommendation 4

We suggest that patients discontinue antiplatelet agents (eg, aspirin, clopidogrel) before undergoing elective hip or knee arthroplasty.

Grade of Recommendation: Moderate

Rationale: Among nonarthroplasty surgical patients, preoperative antiplatelet use predicted higher perioperative blood loss in three studies of moderate to high quality. Reoperation rates due to bleeding varied in only one of the three studies.[23-25]

Although this evidence is not specific to elective hip or knee arthroplasty patients, the work group believes the evidence is still applicable to these patients, who are at risk for bleeding and bleeding-associated complications.

Recommendation 5

We suggest the use of pharmacologic agents and/or mechanical compressive devices for the prevention of VTED in patients undergoing elective hip or knee arthroplasty, and who are not at elevated risk beyond that of the surgery itself for venous thromboembolism or bleeding.

Grade of Recommendation: Moderate

Current evidence is unclear about which prophylactic strategy (or strategies) is/are optimal or suboptimal. Therefore, we are unable to recommend for or against specific prophylactics in these patients.

Grade of Recommendation: Inconclusive

In the absence of reliable evidence about how long to employ these prophylactic strategies, it is the opinion of this work group that patients discuss the duration of prophylaxis with their treating physicians.

Grade of Recommendation: Consensus

Rationale: We recognize the diversity of opinion concerning the clinical importance of DVT as an isolated event or as a surrogate outcome for PE or postthrombotic syndrome, and we understand that for clinical, and sometimes for even medicolegal, reasons, DVT prevention is often the clinician's immediate concern. There is moderate evidence to suggest that pharmacological agents and/or mechanical compression devices reduce DVT rates in patients undergoing elective knee or hip arthroplasty. This is why we are suggesting prophylaxis. Readers of this guideline should recognize, however, that the available, published evidence does not establish whether these prophylactic strategies affect rates of all-cause mortality, fatal PE, symptomatic PE, or symptomatic DVT in patients undergoing elective hip or knee arthroplasty.

We also note that the present recommendation for prophylaxis is of a moderate (rather than strong) grade partly because it is based on a surrogate outcome we do not consider "critical" (we considered major bleeding, pulmonary emboli, and all-cause mortality as "critical," and symptomatic DVT, any DVT, and proximal DVT as not critical). The "critical" outcomes are all patient oriented. The noncritical outcomes are not.

The inability to recommend a specific prophylactic strategy is a direct result of the network meta-analyses we performed. We performed numerous such analyses with sensitivity analyses that included separately analyzing data from patients who underwent hip and knee arthroplasty, analyzing these data combined, and evaluating the impact of study quality on the results, as well as comparing the results of each prophylactic strategy to placebo (or no treatment) and, when placebo/no treatment data were not available, comparing the results of each strategy to results obtained with enoxaparin. The results of these analyses did not consistently suggest that any one strategy is preferable to another.

We also analyzed data on other outcomes but, due to lack of data, network meta-analysis was not possible for them. In total, then, our analyses of the different prophylactic strategies is comprised of 112 high- or medium-quality randomized controlled studies that enrolled patients undergoing elective hip and/or knee arthroplasty. As with the network meta-analyses, the data did not suggest that any specific prophylactic strategy was superior or inferior.

Part of the reason that current data do not permit a conclusion about specific prophylactic strategies is that, in our final network meta-analyses, no pharmacologic agents showed a statistically significant effect in preventing all-cause mortality, symptomatic pulmonary emboli, symptomatic DVT, and major bleeding when data from hip and knee studies were analyzed separately or when they were combined. This may be because these events are rare. In addition, infection rates and reoperations (for any reason) were not reported. Reoperations due to bleeding were reported but were often part of the study authors' definition of major bleeding.

Many of the commonly used agents, such as sodium warfarin and various low-molecular-weight heparinoids, did not show efficacy for preventing VTED. This may be partially explained by the lack of comparison studies with placebo controls and by the rarity of the events of interest. In the final model with PE as the outcome, there were 181 events among 42,390 patients across 25 trials, and only 3 of these trials had a placebo or no prophylaxis arm.

There were a limited number of studies that evaluated mechanical compression devices. In one study on total hip arthroplasties, there was a lower risk of major bleeding in the mechanical group. However, this study was of only moderate quality, partially because only 37% of the compression group had this device alone, with the remainder of the patients receiving low-dose aspirin (81 mg/d), as well.[26] There were also difficulties with the comparability of the control and intervention groups (that some of the studies we examined were not of high quality is another reason why the present recommendation is of moderate strength).

In some analyses of mechanical compression devices studies, less bleeding was found in comparison to no treatment. This may not appear intuitively logical but might be occurring because of problems with randomization and with the patient populations that may not be generalizable to the standard population of patients typically undergoing total hip and knee arthroplasties. The effect may also be occurring for some presently unknown physiologic reasons. Other potentially confounding factors with these studies are enumerated below.

Conclusions about specific prophylactic strategies are also difficult because, in addition to the above-mentioned challenges posed by the rarity of the events of interest and the lack of reporting of critical outcomes, the available studies (1) enrolled a select group of patients and did not necessarily include patients who had a high risk for VTED or bleeding and may not be representative of a typical patient population, (2) used different drug doses (eg, enoxaparin at 30 mg bid versus. 40 mg per day), (3) used different timing of administration of agents (short-term versus longer-term dosing), and (4) used different routes of administration.

Comparing different prophylactic strategies is difficult because there is a paucity of placebo-controlled trials due to early acceptance of prophylaxis being the standard of care.

Finally, we are unable to recommend specific pharmacologic agents and/or mechanical devices. Due to the rarity of the critical outcomes of interest and the limited number of placebo-controlled trials, we had to rely on the analysis of DVT (ie, any DVT), a surrogate measure, to evaluate the relative efficacy of the prophylactic strategies.

Although there is evidence indicating that extending low-molecular-weight heparin use for a total of 28 to 35 days is more effective than stopping low-molecular-weight heparin use after 7 to 10 days for the prevention of symptomatic PE and DVT without increasing major bleeding, the work group noted that the evidence for extending the duration of prophylaxis for other agents is insufficient. Therefore, the work group recommends that patients and physicians discuss the appropriate duration of prophylaxis for each individual situation. This discussion is low cost and consistent with current practice.

As of April 1, 2011, several of the analyzed agents are not approved for marketing or the treatment of any medical condition in the United States. The current policy of the United States Food and Drug Administration (FDA) regarding disclosure of marketing applications can be found in "Current Disclosure Policies for Marketing Applications" on the FDA website.

Recommendation 6

In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who also have a known bleeding disorder (eg, hemophilia) and/or active liver disease, use mechanical compressive devices for preventing venous thromboembolism.

Grade of Recommendation: Consensus

Rationale: As discussed in Recommendation 3, patients who have a known bleeding disorder or active liver disease are at elevated risk for bleeding. Due to the serious complications that can occur in these patients, the work group deemed it appropriate to issue a consensus-based recommendation in spite of a lack of relevant published data. It is the consensus of the work group that mechanical compressive devices are appropriate for these patients as pharmacologic prophylaxis may exacerbate the risk of bleeding. Using mechanical compressive devices is of low risk and consistent with current practice. Consultation with a hematologist or other specialist may be warranted in some cases, especially when a patient is at elevated risk of bleeding and at elevated risk of VTED.

Recommendation 7

In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who have also had a previous venous thromboembolism, receive pharmacologic prophylaxis and mechanical compressive devices.

Grade of Recommendation: Consensus

Rationale: Given that patients who are receiving a hip or knee implant are already at high risk for VTED, a further increase of risk in these patients is of concern. Although none of the studies we located enrolled such patients, the work group deemed that an even greater risk of VTED in these patients justified issuing a consensus-based recommendation for these patients. The consensus of the work group is that both pharmacologic prophylaxis and mechanical compressive devices are appropriate for these patients, assuming that their risk of VTED is greater than their risk of bleeding. Because patients undergoing hip or knee arthroplasty will be receiving some form of prophylaxis anyway, the added costs of using both pharmacologic and mechanical compressive devices will not always be large. Furthermore, the approach in this recommendation is consistent with current practice.

Recommendation 8

In the absence of reliable evidence, it is the opinion of this work group that patients undergo early mobilization following elective hip and knee arthroplasty. Early mobilization is of low cost, is of minimal risk to the patient, and is consistent with current practice.

Grade of Recommendation: Consensus

Rationale: VTED is a potentially catastrophic complication faced by all patients who undergo elective hip and knee arthroplasty. Risk factors that predispose to VTED are embodied by the Virchow triad—hypercoagulability, endothelial injury, and stasis. Early mobilization following hip or knee arthroplasty addresses the stasis limb of the Virchow triad; movement of the operated limb promotes regional blood flow. Mobilization should begin as soon postoperatively as possible. Practices should be in place to ensure that appropriate support is provided throughout the hospital stay to minimize the risk of falls during transfer and ambulation.

Although one moderate-quality study[27] and five low-quality studies compared VTED rates based on timing of mobilization, their results are conflicting. One study of moderate quality suggests that patients mobilizing within 2 to 4 hours of surgery do not have lower VTED readmission rates compared with patients mobilizing the afternoon or evening of surgery. Three low-quality studies suggest that there is no difference in VTED due to timing of mobilization, while two other low-quality studies did find lower rates of PE or VTED readmission among patients who mobilized earlier. Based on the fact that early mobilization has minimal cost, is of low risk to the patient, and is consistent with current clinical practice, issuing a consensus-based recommendation is warranted.

Recommendation 9

We suggest the use of neuraxial (eg, intrathecal, epidural, spinal) anesthesia for patients undergoing elective hip or knee arthroplasty to help limit blood loss, even though evidence suggests that neuraxial anesthesia does not affect the occurrence of venous thromboembolic disease.

Grade of Recommendation: Moderate

Rationale: One high-quality study and two moderate-quality studies addressed neuraxial anesthesia and VTED. None of these studies found a statistically significant difference in outcomes between regional (epidural or spinal) and general anesthesia.

Fifteen randomized controlled trials of high quality and moderate applicability compared perioperative blood loss among patients receiving general, epidural, or a combination of general and epidural anesthesia, or a combination of general anesthesia and lumbar plexus block. There were eight high-quality studies comparing epidural and general anesthesia. Epidural anesthesia resulted in lower intraoperative blood loss. The combination of epidural and general anesthesia resulted in lower intraoperative blood loss compared with general anesthesia alone in two high-quality studies. The combination of lumbar plexus block and general anesthesia resulted in lower intra- and postoperative blood loss compared with general anesthesia alone in two high-quality studies. Hypotensive epidural anesthesia resulted in lower postoperative blood loss compared with spinal anesthesia in two high-quality studies.

Recommendation 10

Current evidence does not provide clear guidance about whether inferior vena cava filters prevent PE in patients undergoing elective hip and knee arthroplasty who also have a contraindication to chemoprophylaxis and/or known residual VTED. Therefore, we are unable to recommend for or against the use of such filters.

Grade of Recommendation: Inconclusive

Rationale: No studies met the inclusion criteria for VTED-related outcomes in arthroplasty patients. Two studies of nonarthroplasty patients compared PE and death rates between patients who received inferior vena cava filters and those who did not. One was a low-quality study of bariatric surgery patients, which found no differences in VTED outcomes between patients with and without inferior vena cava filters. The other was a low-quality study of trauma patients, which reported

lower rates of PE and fatal PE in patients who received inferior vena cava filters. Therefore, based on the limited and conflicting data regarding the benefits of inferior vena cava filters in preventing PE, as well as the fact that none of the studies included arthroplasty patients, we are unable to recommend for or against their use in hip and knee arthroplasty patients.

Future Research

The inability of the available data to distinguish between prophylaxis and no prophylaxis, as well as between different prophylactic regimens, with regard to the critical outcomes (ie, reoperation due to bleeding, death from bleeding, symptomatic PE, death from PE, periprosthetic joint infection, all-cause mortality, reoperation for any reason within 90 days of surgery), in addition to the uncertainty concerning the value of surrogate outcomes (eg, the incidence of DVT) suggests that the approach to conducting clinical trials on thromboprophylactic agents needs to be reexamined. Studies need to be sufficiently powered to detect relatively rare events; the use of registries may help in addressing this requirement. In addition, clinical trials need to report the critical outcomes noted above. Specific areas that the work group targeted for further research include the following:

1. Characterization of risk factors for VTE and bleeding in hip and knee arthroplasty patients;
2. Evaluation of multimodal treatment regimens that combine pharmacoprophylaxis, mechanical prophylaxis, and other modalities (eg, early mobilization, regional anesthesia);
3. Utilization of administrative datasets to obtain the necessary sample size. This would be facilitated by creating codes for the different drugs and mechanical devices used during hospitalization;
4. Utilization of placebo controls in future clinical trials in patients at standard risk of VTED;
5. Utilization of advanced imaging studies (eg, magnetic resonance venography) to establish the presence of DVT in patients with definitive evidence of PE because prior studies that have evaluated the prevalence of DVT with ultrasonography in this population have found a prevalence similar to routine screening;
6. Performance of a meta-analysis of the studies that have attempted to correlate DVT and PE;
7. Performance of studies evaluating the optimal timing and duration of administration of prophylactic agents and/or mechanical compression devices;
8. Performance of focused studies enrolling patients at high risk of VTED or bleeding;
9. Performance of clinical trials in revision hip and knee arthroplasty procedures; and
10. Clarification of the role of inferior vena cava filters in the prophylaxis of high-risk patients.

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